Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 5

	Complete if Known
Application Number	10/579,251
Filing Date	October 20, 2006
First Named Inventor	Luca Gianni
Art Unit	1623
Examiner Name	Jonathan S. Lau
Attorney Docket Number	13566.105020

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number Number - Kind Code[2] (*If known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
/J.L./		US- 20040108086	06/10/2004	Takahashi et al.	
		US- 20040002602	01/01/04	Francesch et al.	
		US- 5,149,804	9/22/1992	Rinehart et al.	
		US- 5,654,426	8/5/1997	Rinehart et al.	
		US- 5,721,362	2/24/1998	Corey et al.	
		US- 5,908,835	06/01/1999	Bissery	
		US- 5,985,876	11/16/1999	Rinehart et al.	
		US- 6,124,293	9/26/2000	Rinehart et al.	
/J.L./		US- 7,241,892	07/10/07	Cuevas et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3] - Number[4] - Kind Code[5] (*If known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
/J.L./		WO 00/69862	11/23/2000	Cuevas et al.		
/J.L./		WO 01/77115	10/18/2001	Flores et al.		
/J.L./		WO 01/87894	11/22/2001	Cuevas et al.		

Examiner Signature	/Jonathan Lau/	Date Considered	07/14/2008

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. [1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 2 of 5

Complete if Known	
Application Number	10/579,251
Filing Date	October 20, 2006
First Named Inventor	Luca Gianni
Art Unit	1623
Examiner Name	Jonathan S. Lau
Attorney Docket Number	13566.105020

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
/J.L./		Burstein et al., "Phase I study of Doxil and Vinorelbine in Metastatic Breast Cancer," Annals of Oncology, vol. 10, pages 1113-1116, 1999, XP8086751	
		Delaloge et al., "Ecteinascidin (ET-743) in heavily pretreated refractory sarcomas: Preliminary evidence of activity," Eur. J. Cancer, vol. 35, suppl. 4, page S271, Abstract No. 1080, Sept 15, 1999	
		D'Incalci et al., "Mode of action of Ecteinascidin-743 (ET-743)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, pages 3872s-3873s, Abstract of Plenary Session 7, November 16-19, 1999	
		European Medicines Agency (EMEA), "Scientific Discussion" from the European Public Assessment Report for Yondelis®, Revision 1, published March 31, 2008, downloaded from the internet on April 2, 2008, from the website <<http://www.emea.europa.eu/humandocs/Humans/EPAR/yondelis/yondelis.htm>>	
		Faulkner et al., "Symbiotic Bacteria in Sponges: Sources of Bioactive Substances," Drugs from the Sea, Fusetani, N. (ed.), Basel Karger, 2000, pp. 107-119	
		Garcia-Carbonero et al., "Population pharmacokinetics of ecteinascidin 743 in patients with advanced soft tissue sarcoma," Clinical Cancer Research, vol. 6, Supplement, Abstract 211, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
		Giovanna et al., "Importance of DNA repair mechanisms for the sensitivity of tumor cells to ET-743," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 303, November 16-19, 1999	
		Gore et al., "Phase I Combination Study of Trabectedin and Capecitabine in Patients With Advanced Malignancies," Poster Presentation, 42nd ASCO Annual Meeting held on June 2-6, 2006, Atlanta, Georgia	
		Hahn et al., "Taxol in Combination with Doxorubicin or Etoposide," CANCER, vol. 72, no. 9, pp. 2705-2711, November 1, 1993	
		Hornicek et al., "In vitro effect of the tetrahydroisoquinoline alkaloid Ecteinascidin-743 (ET-743) on chondrosarcoma (CHSA) cells," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 304, November 16-19, 1999	
/J.L./		Jimeno et al., "Pharmacokinetics (PK)/Pharmacodynamic (PD) Relationships in Patients (PT) Treated With Ecteinascidin-743 (ET-743) Given As 24 Hours Continuous Infusion (CI)," Journal of Clinical Oncology, ASCO Annual Meeting Proceedings, Abstract No. 744, May 15-18, 1999	

/Jonathan Lau/ 07/14/2008

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 3 of 5

Complete if Known	
Application Number	10/579,251
Filing Date	October 20, 2006
First Named Inventor	Luca Gianni
Art Unit	1623
Examiner Name	Jonathan S. Lau
Attorney Docket Number	13566.105020

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
/J.L./		Jin et al., "The antitumor agent Ecteinascidin 743 (ET743), inhibits transcriptional activation of the MDR1 Gene by multiple inducers," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 302, November 16-19, 1999	
		Kovalcik et al., "The Stability of Cyclophosphamide in Lyophilized Cakes. part I. Mannitol, Lactose, and Sodium Biocarbonate as Excipients," Journal of Parenteral Science and Technology, vol. 42, no. 1, Jan-Feb. 1988, pp. 29-37	
		Lopez-Lazaro et al., "Exploratory evaluation of the potential predictors for dose-limiting toxicities (DLTs) in patients treated with Ecteinascidin-743 (ET-743) as a 24-h intravenous (iv) infusion every 3 weeks and its relationship to pharmacokinetics (PK)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3791s, Abstract 308, November 16-19, 1999	
		Lyass et al., "Phase I Study of Doxil-Cisplatin Combination Chemotherapy in Patients with Advanced Malignancies," Clinical Cancer Research, vol. 7, pages 3040-3046, October 2001, XP8086753	
		Manzanares et al., "Advances in the Chemistry and Pharmacology of Ecteinascidins, A Promising New Class of Anticancer Agents," Curr. Med. Chem. - Anti-Cancer Agents, 2001, vol. 1, pp. 257-276	
		Menchaca et al., "Synthesis of Natural Ecteinascidins (ET-729, ET-745, ET-759B, ET-736, ET-637, ET-594) from Cyanosafracin B," J. Org. Chem., published on web October 21, 2003, pp. 8859-8866	
		Rosing et al., "Pharmacokinetics (PK) of Ecteinascidin-743 (ET-743) in three different phase I trials," Proceedings of the American Association for Cancer Research, vol. 40, pp 81, abstract no. 542, March 1999	
		Ryan, D.P. "Studies with Ecteinascidin-743 (ET-743) A Marine Alkaloid," Cancer Invest, vol. 18 (suppl 1), pp 112, abstract no. 87, January 2000, from the Chemotherapy Foundation Symposium XVII Innovative Cancer Therapy for Tomorrow, November 3-6, 1999, New York, NY	
		Sakai et al., "Additional Antitumor Ecteinascidins from a Caribbean Tunicate: Crystal Structures and Activities in vivo," Proc. Natl. Acad. Sci., vol. 89, Dec. 1992, pp. 11456-11460	
		Scotto et al., "Ecteinascidin 743, a novel chemotherapeutic agent that targets transcriptional activation of a subset of genes, including MDR1," Clinical Cancer Research, vol. 6, Supplement, Abstract 210, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
/J.L./		Shertzer et al., "Protection Against Carbon Tetrachloride Hepatoxicity by Pretreatment with indole-3-carbinol," Exptl. Molec. Pathol., vol. 46, pp. 180-189 (1987)	

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 4 of 5

Complete if Known	
Application Number	10/579,251
Filing Date	October 20, 2006
First Named Inventor	Luca Gianni
Art Unit	1623
Examiner Name	Jonathan S. Lau
Attorney Docket Number	13566.105020

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
/J.L./		Shertzer et al., "Protection from N-Nitrosodimethylamine Mediated Liver Damage by Indole-3-carbinol," Exptl. Molec. Pathol., vol. 47, pp. 211-218 (1987)	
		Taamma, A. et al., "Ecteinascidin-743 (ET-743) 24 hours continuous infusion (CI): clinical and pharmacokinetic phase I study in solid tumor patients (PTS). Preliminary Results" 1998 ASCO Annual Meeting Proceedings, Abstract No. 890, 1998	
		Taamma et al., "Ecteinascidin-743 (ET-743) 24 hour continuous intravenous infusion (CI) phase I study in solid tumors (ST) patients (pts)." Proceedings of the American Association for Cancer Research , vol. 39, pp 323, abstract no. 2207, March 1998	
		Taamma et al., "Ecteinascidin-743 (ET-743) in heavily pretreated refractory sarcomas: early results of the French experience," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3791s, Abstract 309, November 16-19, 1999	
		Takebayashi et al., "Multidrug Resistance Induced by DNA Minor Groove Alkylation of Ecteinascidin 743 (Et743)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3851s, Abstract 602, November 16-19, 1999	
		Takebayashi et al., "Nucleotide excision repair-dependent cytotoxicity of Ecteinascidin 743," Clinical Cancer Research, vol. 6, Supplement, Abstract 207, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
		Takahashi et al., "Sequence-dependent Synergistic Cytotoxicity of Ecteinascidin-743 and Paclitaxel in Human Breast Cancer Cell Lines in Vitro and in Vivo," Cancer Research, 62: 6909-6915 (Dec. 1, 2002)	
		Ten Hagen et al., "Pegylated Liposomal Tumor Necrosis Factor-Alpha Results in Reduced Toxicity and Synergistic Antitumor Activity after Systemic Administration in Combination with Liposomal Doxorubicin (Doxil) in soft tissue Sarcoma-Bearing Rats," Int. J. Cancer, vol. 97, pages 115-120, 2002	
		Twelves et al., "Phase I Trials with ET-743, a marine derived (MD) anticancer agent," Eur. J. Cancer, vol. 35, suppl. 4, page S283, Abstract No. 1135, Sept 15, 1999	
		van Kesteren et al. "Clinical Pharmacology of the Novel Marine-derived Anticancer Agent Ecteinascidin 743 Administered as a 1- and 3-h Infusion in a Phase I Study," Anti-Cancer Drugs, Vol. 13, No.4, pgs. 381-393, April 2002	
/J.L./		Weiwei et al., "Potent antitumor activity of ET-743 against human soft tissue sarcoma cell lines," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 305, November 16-19, 1999	

/Jonathan Lau/ 07/14/2008

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 5 of 5

Complete if Known	
Application Number	10/579,251
Filing Date	October 20, 2006
First Named Inventor	Luca Gianni
Art Unit	1623
Examiner Name	Jonathan S. Lau
Attorney Docket Number	13566.105020

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
/J.L./		Zelek et al., "Preliminary results of phase II study of ecteinascidin (ET-743) with the 24 hour (H) continuous infusion (CI) q3week schedule in pretreated" Clinical Cancer Research, vol. 6, Supplement, Abstract 212, pages 4508s-4509s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	

Examiner Signature	/Jonathan Lau/	Date Considered	07/14/2008

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**